REMARKS

Claim Status

Claims 31-38 and 41-50 are pending in the application.

Claims 34, 35, 38, 46 and 47 have been allowed. In this response, dependent claims 34, 35, and 38 have been amended to incorporate all the limitations recited in the independent claims.

Claims 41, 42 and 48 are also amended in this response.

Response to Declaration Filed November 27, 2006

The Examiner contends that the Applicants' opinion and assertion that the lack of *in vivo* data would not lead to a reasonable expectation of success in adapting the method of Li et al. to treat cancer in a subject is without basis. Applicants respectfully traverse.

The Declaration filed November 27, 2006 was filed in response to a rejection under 35 U.S.C. §103(a). The Examiner's response to the Declaration, however, was not directed or pertinent to a rejection under 35 U.S.C. §103(a).

The Examiner's response was addressed to the issue of utility requirement, not the issue of obviousness under 35 U.S.C. §103(a). The Examiner cites:

> ... courts have found ***utility*** for therapeutic inventions despite the fact that an applicant is at a very early stage in the development of a pharmaceutical product ... We perceive no insurmountable difficulty, under appropriate

> circumstances, in finding that the first link in the screening chain, in vitro testing, may establish a practical ***utility*** for the compound … The Federal Circuit has reiterated that therapeutic ***utility*** sufficient under the patent laws is not to be confused with the requirements of the FDA with regard to safety and efficacy of drugs to marketed in the United States. FDA approval, however, is not a prerequisite for finding a compound ***useful*** within the meaning of the patent law. … The stage at which an invention in this field becomes ***useful*** is well before it is ready to be administered to humans. (emphasis added)

It is apparent that the above quotation cited by the Examiner is addressing the establishment of utility under the patent law by *in vitro* testing in the context of pharmaceutical inventions. The above citation does not address any standard related to the issue of obviousness under 35 U.S.C. §103(a), e.g. motivation to combine references and reasonable expectation of success.

The Examiner has not provided any response to Applicants' assertion that whether a drug or composition will be useful in clinic can only be determined by vigorous clinical trials. In the Declaration filed November 27, 2006, Applicants have provided ample and convincing evidences to support the above assertion. For example, Flavopiridol, an inhibitor of several cyclin-dependent kinases, exhibited potent growth-inhibitory activity against prostate cancer cells *in vitro* (Li et al., Int. J. Oncol. 17:755-759 (2000)). However, results from clinical trial indicated that Flavopiridol was ineffective in patients with previously untreated metastatic hormone-refractory prostate cancer (Liu et al., Clinical Cancer Research 10:924-928 (2004)).

Another example in the Declaration is endostatin, the famous angiogenesis inhibitor that inhibited endothelial cell proliferation *in vitro*, and even caused primary tumor regression in animal model (O'Reilly et al., Cell 88:277-285 (1997)). However, results from a Phase I clinical trial with patients having refractory solid tumors indicated that no clinical response was generated by using endostatin, even though endostatin was well tolerated (Thomas et al., J. Clinical Oncol. 21:223-231 (2003)). Similarly, endostatin also failed in a Phase II clinical trial with patients having advanced neuroendocrine tumors (Kulke et al., J. Clinical Oncol. 24:3555-3561 (2006)).

Hence, in view of the above data regarding *in vitro* data and clinical success, one of ordinary skill in the art would readily recognize that whether a drug or composition will be useful in clinic can only be determined by clinical trials. The Examiner has not provided any reason why one of ordinary skill in the art would perceive a reasonable expectation of success based on *in vitro* data only in spite of the examples stated in the Declaration.

In conclusion, Applicants reiterate that in view of the general knowledge as stated in the Declaration filed November 27, 2006, the *in vitro* data of Li et al. do not provide one of ordinary skill in the art a reasonable expectation of success in using aqueous chinesis extract to treat cancer in a subject. In other words, whether a drug or composition will be useful in clinic can only be determined by clinical trials.

Rejection Under 35 U.S.C. §112, 1st Paragraph, Enablement

Claims 41, 42 and 48 are newly rejected under 35 U.S.C. §112, 1st paragraph, for lack of enablement. The Examiner contends that the specification, while being enabling for a method wherein the therapeutic microtubule-destabilizing agent is the taxol-like nocodazole, does not reasonably provide enablement for a method wherein the therapeutic microtubule-destabilizing agent is any taxol compound. The rejection is respectfully traversed.

In order to expedite the prosecution of this application, Applicants have amended claims 41, 42 and 48 to recite "taxol-like nocodazole compound". Accordingly, Applicants submit that the claims have been amended to obviate the rejection, and it is respectfully requested that the rejection of claims 41, 42 and 48 under 35 U.S.C. §112, 1st paragraph, be withdrawn.

Rejection Under 35 U.S.C. §103(a)

1. Claims 31 and 32 remain rejected under 35 U.S.C. §103(a) as being unpatentable over Li et al. (2000) for reasons of record set forth in the Office Action mailed September 26, 2006. The rejection is respectfully traversed.

2. Claims 31-33, 36, 37, 43, 44, 45, 49 and 50 are newly rejected under 35 U.S.C. §103(a) as being unpatentable over Li et al. (2000) in view of Zhang et al. (1990). The rejection is respectfully traversed.

The above two rejections are based on the primary reference of Li et al. As discussed above, Applicants assert that Li et al., which only provide *in vitro* data, do not provide one of ordinary

skill in the art a reasonable expectation of success in using aqueous chinesis extract to treat cancer in a subject in view of the knowledge generally available in the art as stated in the Declaration filed November 27, 2006.

In the office action mailed September 26, 2006, the Examiner contends that

> "it would have been obvious to one of ordinary skill in the art at the time of the invention to have used the method of Li et al. for inhibiting the cell growth in human cancer cells by administering an effective amount of aqueous chinesis extract as a treatment of a solid tumor in a subject because the herbal extract was shown to inhibit cancer cell growth *in vitro*."

The Examiner, however, has not provided any reason why one of ordinary skill in the art would perceive a reasonable expectation of success based on *in vitro* data only in spite of the failed examples stated in the Declaration filed November 27, 2006.

CONCLUSION

In view of the above remarks, Applicants submit that the Examiner has not established a *prima facie* case of obviousness, and it is respectfully requested that the above rejections under 35 U.S.C. §103(a) be withdrawn.

If a telephone interview would be of assistance in advancing the prosecution of the subject application, Applicants' undersigned attorney invites the Examiner to telephone him at the number provided below. If any additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 50-1891.

Respectfully submitted,

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